Effects of motoneuron properties on reflex stability in spastic subjects: a simulation study

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Abstract – **The influence of motoneuron pool properties on the stability of the stretch reflex at the ankle in subjects with spinal cord injury was tested using a comprehensive model of the reflex pathway. This model included the passive and active components of the triceps surae muscles, muscle spindles, neural transport delays, limb mechanical properties, and a lumped parameter model of the motoneuron pool input-output relationship. Simulations show that as the motoneuron firing threshold was reduced (reflecting increased excitability of spinal motoneurons), normal reflex responses became unstable and oscillations developed similar to those observed in spastic patients. In parallel, when reflex delay times typical for triceps surae in man were chosen, and motoneuron excitability increased progressively, oscillatory ankle movements were readily elicited. Conversely, as pathway delays were reduced, reflex stability increased, as the oscillatory behavior usually damped out. Decreases in motoneuron pool synaptic gain had a stabilizing effect on the reflex response, as low motoneuron gains tended to eliminate oscillatory behavior. Using an Absolute Stability Analysis, we found that reflex pathways containing long neural transport delays and muscles with slow dynamics tended to place the largest stability constraints on the motoneuron pool. These findings support the hypothesis that unstable oscillatory behavior, such as the oscillations observed in clonus, will occur when the motoneuron excitability increases in a reflex pathway containing long delays.**

Key words – **spasticity, clonus, reflex, muscle, spinal cord injury**

I. INTRODUCTION

An extension of spasticity, referred to as clonus [1,3,9,10], is a behavior in which certain limb segments will move in an oscillatory fashion at frequencies ranging between 4 and 6 Hz. For many years, a common belief has been that clonus is simply a repetitive stretch reflex manifested in a high gain, feedback circuit [3,4,9]

There has been a resurgence of support over the last couple of years for the role of a central pattern generator driving these rhythmic movement patterns in spastic subjects [2]. Harkema et al. (1997) demonstrated that rhythmic firing patterns in SCI subjects occurred while their lower limbs were driven through kinematic trajectories mimicking those that occur in natural human gait. In these experiments, they found that there was activity in muscles such as the tibialis anterior muscles that did not correlate with the lengthening of the muscle. They concluded that clonus could not be driven through a series of repetitive stretch reflex responses but instead was the emergence of a central pattern generator exposed after SCI. This theory is not new; others have also proposed that a spinal generator drives clonus and has little [1] or no dependence [11] on peripheral conditions.

In our previous modeling work [3] we demonstrated that clonus could arise in the stretch reflex circuit if the level of motoneuron excitability increased in a reflex pathway containing significant delays (attributed to neural conduction time and perhaps to phase lags associated with the low-pass filtering properties of the muscle). The primary limitation was that many of the parameters within the model were derived from healthy control subjects. As was shown in [5], muscle properties undergo profound changes after spinal cord injury, such that the accuracy of our previous simulations may have been compromised. Furthermore, experimental observations of clonus input-output data are needed to establish how the stretch reflex properties would be affected by various conditions, such as limb loading or changes in joint kinematics. This information is essential for establishing the credibility and reliability of a model representing such a complicated system.

By coupling an experimentally identified muscle model with a knowledge of neural conduction delays determined in H-reflex tests, inertial estimates of the foot, and applying a physiologically based model of the muscle spindles, our goal was to better understand how the properties of the motoneuron pool might change after SCI leading to reflex instability.

II. METHODS

2.1 Model of the stretch reflex pathway

The model of the ankle stretch reflex pathway is shown in Figure 1, and is comprised of components representing the active and passive muscle properties, a neural conduction delay, muscle spindles, inertial properties of the limb, and finally a lumped representation of the motoneuron pool. Each of the model components was derived experimentally or selected from the literature.

2.2 Muscle model

Muscle activation dynamics were represented by a first-order differential equation while a modified Hill model [6] was used to determine contractile element velocity during both shortening [6] and lengthening [8]. The torque-angle relation was represented by a nonlinear scaling function that ranged in value from 0 to 1. The series elastic element (SE) was treated as a combined representation of muscle and tendon stiffness, and was modeled as a quadratic function. Finally, The passive dynamics was estimated using a visco-elastic element. The

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total torque resisting muscle stretch was then the sum of the active torque driven by the reflex pathway

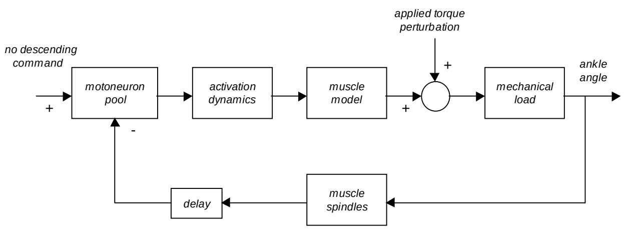

Figure 1. Model of the ankle stretch reflex pathway.

and the passive torque generated by the kinematics of the ankle joint.

2.3 Spindle model

The muscle spindle model used was a modified version of the structure originally based on the work of Houk et al. (1981), where the spindle firing rate is related to the ankle position and velocity as:

$$S_{fr} = G_1 * (\theta - \theta_s) + G_2 \dot{\theta}^{0.5}$$

where G_1 and G_2 represents the spindle gains, θ is the joint angle, θ_s is the spindle slack angle, and $\dot{\theta}$ is the ankle joint velocity.

2.4 Motoneuron pool

The motoneuron pool transformation establishes a scaling function representing muscle activation, which ranges between 0 and 1, and is a function of the amount of spindle input to the motoneuron pool. The input-output relation for the lumped motoneuron pool was represented by a Gaussian cumulative distribution function. Motoneuron threshold was the amount of input at which the motoneuron relationship began to rise while the motoneuron pool gain was a measure of the rate of rise (or slope).

2.5 Model setup

Reflex simulations were conducted using the model described above with experimentally derived parameters for most of the components. Torque inputs to the model were the same as those used experimentally in [4] to elicit clonus in spinal cord injured subjects so that direct comparisons could be drawn between the model behavior and observed stretch reflex behavior. The only true unknown in the model was the motoneuron pool input-output relationship, thus simulations were run while varying motoneuron properties over a wide spectrum, in order to investigate their influence on model output.

2.6 Stability analysis of motoneuron I-O boundary conditions

Because there is no direct way of measuring the motoneuron pool input-output relationship in man, we utilized the Circle Criteria to provide boundary conditions in which the system would remain stable. With the exception of the motoneuron pool, each element in Figure 1 was first linearized in order to form the control circuit shown in the upper trace of Figure 2. In this setting, spindle firing rate acted as the input to *N(e)* and muscle activation as the output. The Circle Criteria is based on the assumption that the nonlinear element, *N(e)*, is bounded by a sector as shown in Figure 2 (lower trace). By determining k_1 and k_2, we could derive constraints on the motoneuron pool so that the system would remain asymptotically stable.

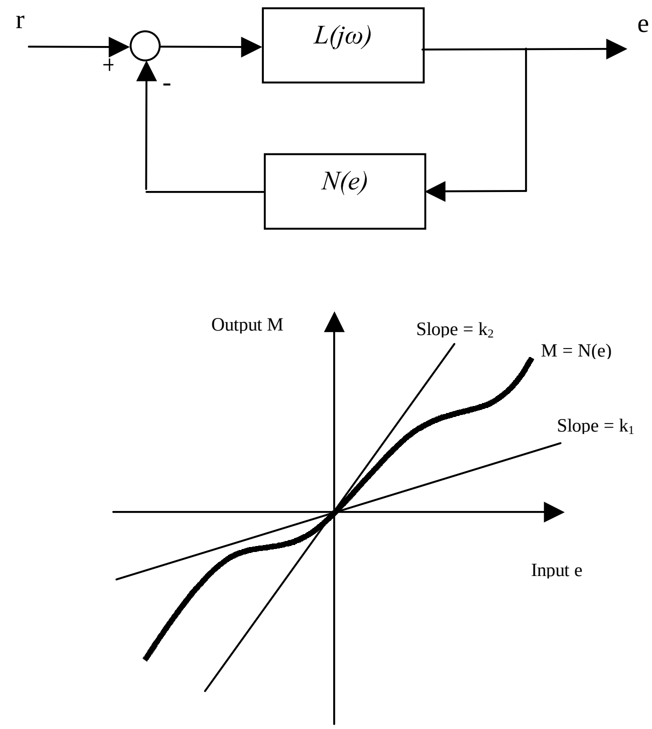

Figure 2 *Schematic of feedback control system with a single nonlinearity in the feedback pathway It is assumed that this nonlinear element is bounded within the sector shown in the lower trace.*

III. RESULTS

Using the model shown in Figure 1, we first tested the stability of the stretch reflex response to changes in motoneuron threshold, motoneuron gain, and neural transport delay. A stability analysis was then done to determine the necessary boundary conditions that would guarantee asymptotic stability for the system.

3.1 Effects of motoneuron pool threshold

Using the same torque inputs as used experimentally [], we varied the motoneuron threshold over a wide range of values while holding all other parameters constant, and we evaluated how threshold changes affected the stretch reflex response.

Figure 3 depicts the resulting kinematic traces for three different motoneuron threshold values. In the upper trace, the threshold resides at a value such that the majority of torque

resisting muscle stretch arises from the passive joint mechanics. As a result, the ankle moves rapidly into dorsiflexion following the onset of the ramp torque input, and quickly reaches a steady-state value. The small oscillations arise because of the slightly under-damped passive properties of the ankle joint. This type of response would be expected from a relaxed, healthy control subject where there would be little or no reflex response for a stretch of this speed and amplitude.

As the motoneuron threshold is reduced, the stability of the system begins to break down, manifested by the appearance of brief oscillations. Further reductions in threshold results in sustained oscillations where the frequency of oscillation is just under 5 Hz at an amplitude of nearly 18^o, both of which are similar to that collected experimentally [4].

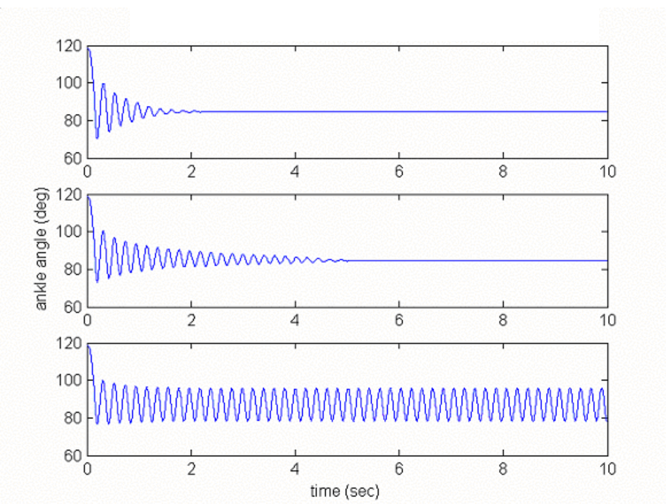

Figure 3. Influence of motoneuron firing threshold on the stretch reflex response. Top trace is for high threshold, where majority of resistance to stretch arises from passive joint mechanics. As the threshold is reduced, oscillatory behavior arises, with movement frequencies of 5 Hz and an amplitude between 15-20 degrees.

The essential features of the predicted reflex response can be described in the following manner. After each muscle contraction, the muscle will relax and lengthen due to the persistent load applied to the foot. As a result, the spindles will fire generating another reflex response and ankle plantar flexion. This pattern of events leads to the same type of oscillatory movements observed in spastic subjects. It is only at a low threshold value that the spindle firing generated during the lengthening phase of movement is able to reach motoneuron activation threshold allowing for the generation of rhythmic muscle contractions.

3.2 Effects of motoneuron pool

In order to test gain influences on reflex behavior, we ran simulations at various levels of motoneuron gain. Starting with motoneuron threshold and gain values that resulted in sustained oscillations (lower trace of Figure 3), the motoneuron gain was incrementally decreased with the resulting behavior illustrated in Figure 4. Similar to the influence of increasing motoneuron firing threshold, decreases in motoneuron gain tended to stabilize the reflex response. In this capacity, the amount of spindle input generated during the lengthening phase of clonus is adequate to reach motoneuron firing, however because the gain of the pool is low, the amount of force generated by the corresponding motoneuron activation is not large enough to continuously overcome the applied load and plantar flex the foot.

3.3 Effects of neural transport delay

Starting with model parameters that resulted in sustained clonus, we systematically decreased the delay, which is equivalent to shortening the length of the monosynaptic reflex pathway. In Figure 5, we show how decreasing the neural transport delay tends to stabilize the system. In this capacity, as the muscle begins to stretch

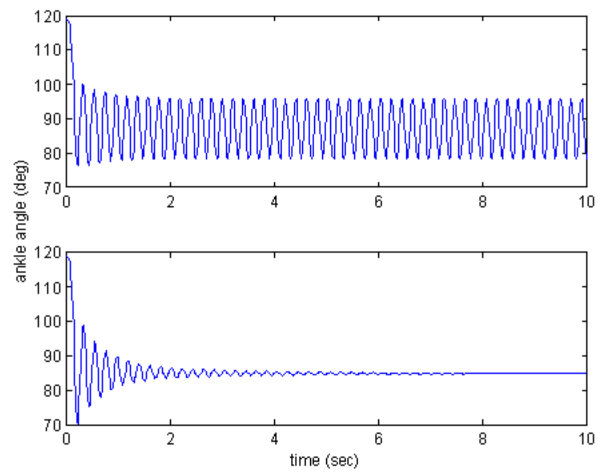

Figure 4. Influence of motoneuron gain on the stretch reflex response. In the upper trace, the model predicts sustained oscillatory movements similar to those observed in spastic subjects. When the motoneuron gain was decreased while all other parameters were held constant, the reflex response stabilizes.

because of the externally applied load, the reflex will come on during muscle stretch and begin resisting the external perturbation rather than adding a phase of movement.

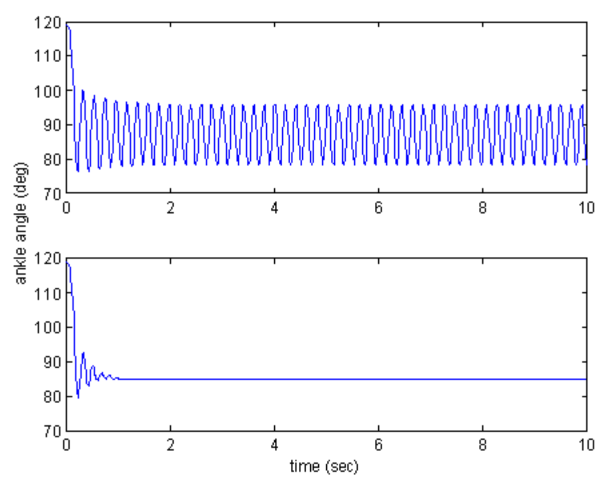

Figure 5. Effects of decreasing neural transport delay. In the upper trace, the delay is set to 35 ms, a value derived experimentally for SCI subjects. When this delay is reduced to 15 ms, the reflex response stabilized and does not produce rhythmic movements. This is demonstrated in the lower trace.

3.4 Motoneuron pool boundary conditions for stability

The limits on feed-back gain were determined by plotting *L(jω)* on the Nyquist plane and determining the maximum sector in which the nonlinear motoneuron pool function could reside while simultaneously guaranteeing stability. Figure 6 illustrates how the motoneuron pool I-O function is bounded within such a sector. Analyzing the system across a wide range of parameters, we found that the tightest stability constraints on the motoneuron pool function (e.g. smaller shaded area) occurred in reflex pathways containing long neural transport delays and muscles that were dominated by slow twitch properties.

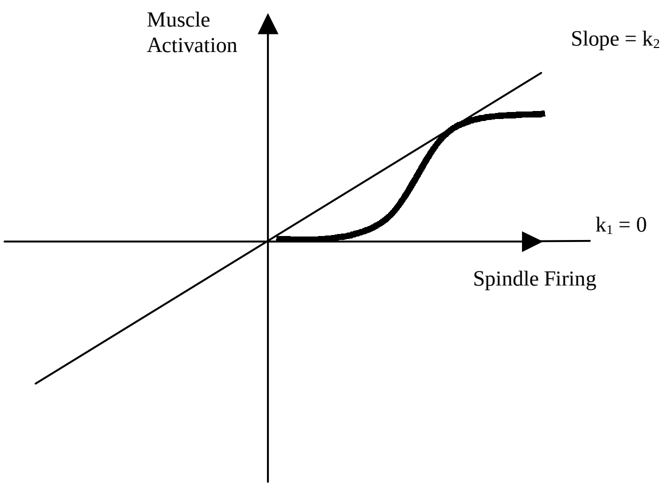

Figure 6. Stability bounds illustrating how the motoneuron pool input-output function is contained within the region defined by k_1 and k_2. The system L(jω) will remain stable for any time-varying nonlinearity which lies within this sector.

IV. DISCUSSION

Using a detailed model of the stretch reflex pathway, we found that sustained oscillations comparable to those that occur in spastic subjects arise when two conditions are present. First, there must be significant neural conduction delays in the reflex pathway, so that reflex responses to imposed perturbations will come following rather than during muscle stretch. And second, motoneuron threshold and/or gain must be such that the spindle activity generated during muscle lengthening will be sufficient to reach motoneuron threshold and generate substantial motoneuron firing. The fact that clonus and spasticity coexist is not surprising, as clonus appears to be an extension of spasticity. That is, in many lesions of the neuraxis, such as in stroke or SCI, there appear to be alterations in the net inhibition of segmental neurons. As a result, the motoneurons will become hyperexcitable, since they will sit closer to their recruitment thresholds. A smaller amount of excitatory synaptic input will then elicit motoneuron firing. Clonus then emerges when increased motoneuron excitability occurs in muscles with long neural transport delays. The destabilizing effects of the neural delay were shown both in the simulations as well as the Circle Criterion stability analysis.

As discussed in the introduction, some authors have proposed that clonus is not due to a self-reexcitation of hyperactive stretch reflexes but instead reflects the emergence of a central pattern generator [1,2,11]. We do not favor the central pattern generator for numerous reasons. First, as we demonstrated in our previous work [4], the kinematics and muscle activity during clonus are strongly dependent on external conditions. That is, as we increased the loading on the foot, there was a direct correlation between the magnitude of the applied load and the resulting movement/burst frequencies. If clonus was driven by central mechanisms independent of the stretch reflex, then this would not occur. The fact that clonus has the behavior of a stable limit cycle may explain the inability of previous investigators to change the kinematics of the oscillations.

Summary and Conclusions

We conclude that following lesions to the CNS, motoneuron excitability increases (by way of decreased motoneuron current threshold and/or modest increases in motoneuron gain) and when combined with significant loop delays, clonus will occur. Furthermore, we have shown that sustained oscillations can occur in a reflex pathway through self re-excitation, which contradicts the hypothesis that a spinal generator must be involved in clonus.

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